Citation:

Noakes M, Foster PR, Keogh JB, James AP, Mamo JC, Clifton PM. Comparison of isocaloric very low carbohydrate/high saturated fat and high carbohydrate/low saturated fat diets on body composition and cardiovascular risk. *Nutr Metab* (Lond). 2006 Jan 11; 3:7.

PubMed ID: 16403234

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare, under isocaloric conditions, the effects of a very-low-carbohydrate (CHO) diet to two, low-saturated fat, high-CHO diets on body composition and cardiovascular risk.

Inclusion Criteria:

- At least one cardiovascular risk factor
- BMI greater than 28kg/m^2.

Exclusion Criteria:

Not described.

Description of Study Protocol:

Recruitment

Subjects were recruited by public advertisement.

Design

- Randomized controlled trial that lasted 12 weeks
- Subjects were matched on the basis of age, gender and BMI before being randomly assigned to one of three dietary intervention groups.

Dietary Intake/Dietary Assessment Methodology

Subject completed food checklists, as well as three-day weighed food records every two weeks to

assess dietary compliance throughout the 12-week study.

Blinding Used

Not applicable.

Intervention

- All three diets were designed to be isocaloric and 30% energy restricted for eight weeks, followed by four weeks on the same macronutrient proportions, but maintaining energy balance
- Key foods for each diet (approximately 36% of total energy) were supplied to subjects every two weeks (uncooked and pre-weighed)
- Subjects were counseled by a dietitian on the dietary protocol and on how to keep dietary-intake checklists for all foods consumed each day over the study duration
    - The very-low-fat diet was 70% CHO, 10% fat, 20% protein
    - The high-unsaturated fat diet was 50% CHO, 30% fat, 20% protein
    - The very-low-CHO diet was 4% CHO, 61% fat, 35% protein.

Statistical Analysis

- Baseline measurements were assessed using two-factor ANOVA with diet and gender as the fixed factors
- The effect of the diet intervention was assessed using repeated-measures ANOVA, for each dependent variable, the measurements at weeks zero, four, eight and 12 are the within subject factors and diet and gender are the between subject factors
- When significant time-by-diet effects were found, post hoc sub-group analysis was performed using Tukey's test
- The study had 80% power (α=0.05) to detect differences between dietary groups of 3.6kg in body weight, 0.9kg in lean and fat mass, 3mU/L in fasting insulin and 0.2mmol/L in LDL-cholesterol
- Significance was set at $P<0.05$.

Data Collection Summary:

Timing of Measurements

- Subjects body weight and dietary intake checklists and food records were monitored every two weeks
- Blood and urine samples, as well as measures of body composition and an oral glucose tolerance test, were taken at baseline and at the end of 12 weeks.

Dependent Variables

- Body weight was measured by study personnel
- Blood samples were taken to assess plasma glucose, insulin, ketones and lipid concentrations. Homocysteine, folate, B_{12}, and CRP concentrations were also measured
- 24-hour urine samples were collected to assess urea/creatinine ratio, calcium, sodium, potassium, deoxy-pyridinoline/creatinine ratio and pyridinoline/creatinine ratio
- Venous blood samples of glucose, insulin and free fatty acid concentrations were taken after an oral glucose-tolerance test and a meal tolerance test
- Body composition was measured by whole body DEXA

- Blood pressure was measured by study personnel.

Independent Variables

Dietary intake data was collected using food checklists and three-day food records.

Control Variables

Not applicable.

Description of Actual Data Sample:

- *Initial N:* N=83
  - N=28 very-low CHO diet (VLC) group
  - N=28 very-low fat (VLF) group
  - N= 27 high-unsaturated fat (HUF) group
- *Attrition (final N):* N=67
  - N=24 VLC group
  - N=22 VLF group
  - N=21 HUF group
- *Age:*
  - 48.4±8.0 years VLC diet group
  - 50.7±10.3 years VLF group
  - 46.1±9.5 years HUF group
- *Ethnicity:* Not described
- *Other relevant demographics:* Not described
- *Anthropometrics:*
  - 32.5±3.1kg/m^2 VLC diet group
  - 32.6±4.0kg/m^2 VLF group
  - 33.4±3.6kg/m^2 HUF group
- *Location:* Australia.

Summary of Results:

- Percent fat mass loss was not different between diets
  - Very-low CHO (VLC): -4.5±0.5
  - Very-low fat (VLF): -4.0±0.5
  - High-unsaturated fat (HUF): -4.4±0.6kg
- Lean mass loss was 32-31% on VLC and VLF compared to HUF (21%) ($P<0.05$)
- LDL-cholesterol increased significantly only on VLC by 7% ($P<0.001$ compared with the other diets), but apoB was unchanged on this diet and HDL-cholesterol increased relative to the other two diets
- Triacylglycerol was lowered by 0.73±0.12mmol/L on VLC compared to -0.15±0.07mmol/L on HUF and -0.06±0.13mmol/L on VLF ($P<0.001$)
- Plasma homocysteine increased 6.6% only on VLC ($P=0.026$)
- Very-low CHO lowered fasting insulin 33% compared to a 19% fall on high-unsaturated fat and no change on VLF ($P<0.001$).
- The VLC meal also provoked significantly lower postprandial glucose and insulin responses than the VLF and high-unsaturated fat meals

- All diets decreased fasting glucose, blood pressure and CRP (P<0.05).

Author Conclusion:

Isocaloric very-low CHO diets results in similar fat loss than diets low in saturated fat, but are more effective in improving triacylglycerols, HDL-cholesterol, fasting and postprandial glucose and insulin concentrations.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	No
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	No
2.2.	Were criteria applied equally to all study groups?	???

2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	???
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes

5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	No
6.6.	Were extra or unplanned treatments described?	No
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	???
7.6.	Were other factors accounted for (measured) that could affect outcomes?	No
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes

8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	No
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	No
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes